ŤAHYŇA VIRUS INFECTION IN MICE IMMUNOSUPPRESSED WITH CYCLOPHOSPHAMIDE

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Cyclophosphamide (CPA) may enhance mortality in mammals infected with arboviruses of the families *Togaviridae* (*1, 2*) and *Orbiviridae* (*3*). The effect of CPA on infections caused by bunyaviruses has not yet been studied. We report a CPA-mediated fatal CNS infection with Ťahyňa (TAH) virus (*Bunyaviridae*; California group) of adult mice which are otherwise resistant to this virus.

Exp. 1. Randombred 6-wk-old SPF male (28.9 ± 2.4 g) and female (25.5 ± 2.3 g) ICR mice (Velaz, Prague) were given intraperitoneally (i.p.) either 80 mg/kg body-weight of CPA (VEB Jenapharm Ankerwerk, Rudolstadt) in 0.15 ml saline, or 0.15 ml saline alone. The mice were infected i.p. one day later each with $10^{3.74}$ $SMicLD_{50}$ of TAH virus strain T 16 (*4*) at its 3rd suckling mouse (SM) brain passage level, suspended in 0.2 ml of phosphate buffered saline with 0.75 % bovine serum albumin ("diluent"). Control mice received i.p. 0.2 ml diluent. Blood sera were collected 21 days later and tested in a plaque-reduction neutralization microtest (PRNT) on XTC-2 cells (*5*). The CPA treatment resulted in a 2-fold decrease of VN antibodies in 16 male (titre 512) and 16 female (titre 1024) mice infected with TAH virus, compared with the CPA-untreated infected 16 males (titre 1024) and 16 females (titre 2048). All the 64 infected mice survived the observation period (21 days p. i.) though low amounts ($< 10^{2.7}$ $SMicLD_{50}$/g) of TAH virus were recovered from the brains of CPA-treated animals 21 days p. i. by intracerebral (i. c.) inoculation of SM, while no virus was detected in the brains of CPA-untreated infected mice. Moreover, the infected CPA-treated animals demonstrated a significantly ($P < 0.05$) lower (ca. 20 %) weight increase than those infected but CPA-untreated. The weight gain of the mice CPA-treated and uninfected (9 males, 10 females) was equal to that of the infected CPA-untreated animals.

Exp. 2. Randombred 4-wk-old SPF male ICR mice (21.7 ± 1.7 g) were infected i. p. with $10^{4.50}$ $SMicLD_{50}$ of the same virus in 0.2 ml diluent, while control mice received 0.2 ml diluent. The animals were then given two i. p. injections (2 and 5 days p. i.) of either CPA (130 and 160 mg/kg, respectively) in 0.2 ml saline, or saline alone. The double dose of CPA resulted in an acute, fatal encephalitis of all 12 infected mice compared to an inapparent infection of 12 mice infected but CPA-untreated. Average survival time of the infected CPA-treated mice was 12.1 days (range 9-15 days), and the brains of dead mice contained $10^{7.32}$ $SMicLD_{50}$/g of TAH virus when pooled, with the individual range from $10^{4.20}$ to $10^{5.75}$ PFU/g found by a plaque assay on XTC-2 cells. On the other hand, no virus was detected in the brains of the 12 infected but CPA-untreated mice killed 15 days p. i. No mortality or central nervous system disease symptoms occurred among the 10 CPA-treated but uninfected mice. In the heart blood plasma of 2 dead (13th day p. i.) randomly selected CPA-treated infected mice, no antibodies against TAH virus were detected in PRNT, while antibody titres of 512 and 1024 were found in the plasma of 2 killed (15th day p.i.) CPA-untreated infected mice.

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